



# Anatomic and non-anatomic substrates in infants with two ventricles undergoing aortic arch repair

## Original Article

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### Abstract

**Objectives:** We sought to examine the relative importance of surgical lesion complexity versus the presence of genetic/syndromic/extracardiac anomalies (GSAs) in determining survival, morbidity or need for reinterventions following repair for aortic arch hypoplasia. **Methods:** A single-centre, retrospective cohort study of infants undergoing biventricular aortic arch repair *via* sternotomy from 2010 to 2021 was conducted. Survival analysis was performed using Kaplan–Meier methods, with additional Bayesian survival modelling for subgroups. Composite morbidity comprised respiratory, renal, neurologic, or sepsis-related complications. **Results:** Of 83 included infants,  $n = 13/83$  (15.7%) had complex repairs; 27/83 (32.5%) were GSA+. Operative mortality was significantly higher in GSA+ versus GSA– patients (18.5% vs. 1.8%;  $p = 0.01$ ), though not for complex versus non-complex repairs. Overall 10-year Kaplan–Meier survival was 86.7%. Bayesian modelling suggested equivalent post-discharge attrition in non-complex/GSA+ and complex/GSA– patients, with the poorest outcomes in complex/GSA+ patients; non-complex/GSA– patients had 100% survival. GSA+ patients exhibited higher composite morbidity (44.4% vs. 7.1% in GSA–  $p < 0.001$ ), with their mode of death seemingly related to a high incidence of respiratory and neurological morbidity, notably in Dandy–Walker syndrome. The 10-year freedom from arch reinterventions was 87.7%; neither complexity, GSA status, nor post-repair peak arch velocity predicted the need for arch reinterventions. **Conclusions:** Whilst anatomic complexity may have been somewhat neutralised as a risk factor for operative mortality, in contrast to GSA+ status, there is further post-discharge attrition attributable to complexity or GSA+ status, with additive risk effects. Morbidity directly related to certain syndromes underlies some of this risk. Non-anatomic substrates represent a persistent limitation to outcomes of surgical aortic arch repair in infants.

## Introduction

For many congenital cardiac surgical repairs, anatomic substrates involving constellations of structural anomalies and/or smaller patients and more diminutive structures are less limiting in achieving favourable outcomes than in previous eras.<sup>1,2</sup> Non-anatomic substrates, however, particularly in the form of genetic/syndromic/extracardiac congenital anomalies (GSAs), still present potential challenges.<sup>3–5</sup> Few studies, however, have attempted to dissect out the relative effects of surgical lesion complexity versus the presence of GSAs on outcomes of aortic arch repair in 2-ventricle patients.

We were aware of a relatively high incidence of GSAs in the surgical population presenting with aortic arch hypoplasia at our institution and therefore sought to examine the relative importance of surgical anatomic complexity versus the presence of GSAs in determining outcomes of survival, morbidity, or need for arch reintervention following 2-ventricle repair for aortic arch hypoplasia. We further sought to determine whether perioperative factors could account for any observed differences.

## Patients and methods

### Study cohort and subgroups

We performed a single institution, retrospective cohort study from 2010 to 2021 of all infants undergoing aortic arch reconstruction *via* median sternotomy. Single ventricle patients and redo arch repairs were excluded. Arch repair *via* median sternotomy was performed in patients

with proximal transverse arch dimension  $< \text{weight (kg)} + 1 \text{ mm}$  according to Melbourne criteria, and arch dimensions are therefore described in mm rather than  $z$ -scores.<sup>6,7</sup>

Electronic medical records were interrogated for patient demographics, intraoperative data, survival status, major morbidity, or need for catheter or surgical arch reintervention. Prematurity was defined as gestation at delivery  $\leq 36$  weeks.<sup>3,8</sup> Data were also extracted on the preoperative status of patients including preoperative shock or need for mechanical ventilation. Follow-up for the study was completed at the end of 2023. The study had been approved by the Institutional Research Board (IRB), and the need for informed consent had been waived (IRB Approval #: 2024.020-BSJCH).

Primary outcomes of survival (including hospital mortality as defined by the Society of Thoracic Surgeons)<sup>5</sup> and perioperative morbidity were studied for the entire cohort as well as for non-complex/complex or GSA-/GSA+ patients. Further exploratory survival analysis was then performed on 4 subgroup classifications: non-complex/GSA-; non-complex/GSA+; complex/GSA-; and complex/GSA+.

Non-complex patients underwent arch repair with/without ventricular septal defect or complete atrioventricular canal only.<sup>2</sup> Complex lesions included those with double outlet right ventricle; transposition of great arteries, with or without interrupted aortic arch; and patients requiring extensive bilateral pulmonary artery reconstruction. We included pre- and postoperative echocardiographic measurements for aortic arch segments and peak arch velocities prior to hospital discharge.

All patients had formal genetic analysis. Composite morbidity comprised renal, respiratory, neurological complications and sepsis. Identification of patients with vocal cord paresis was done on initial clinical symptoms and confirmed on indirect bedside flexible laryngoscopy. Since 2020, all patients have undergone routine post-arch repair laryngoscopy.

### Surgical technique

All patients underwent aortic arch reconstruction involving excision of ductal tissue with end-end reconstruction of the posterior wall at this level if required and patch augmentation of the arch around to the mid-ascending aorta. A pulmonary homograft patch was used in 80/83 patients and glutaraldehyde-treated pericardium in 2 patients; an isolated arch advancement was performed in 1 patient. Concomitant procedures for repair of double outlet right ventricle or transposition of great arteries were performed as indicated. Our cardiopulmonary bypass strategy consisted of moderate-deep hypothermia with systemic cooling to 24–28 degrees Celsius together with selective antegrade cerebral perfusion (79/83 patients; isolated deep hypothermic circulatory arrest at 18–20 degrees Celsius was used in 4 patients) with placement of the arterial cannula either directly into the innominate artery or *via* a 3.5 mm GoreTex™ shunt (W. L. Gore & Associates, Newark, DE, USA). Del Nido cold blood cardioplegia was used for all cases.

### Statistical analysis

Continuous data were reported as medians with the interquartile range with comparison between groups using the Mann–Whitney  $U$  test. Categorical data were expressed as proportions and compared between groups using Fisher's exact test. Kaplan–Meier analysis and log-rank test were used to evaluate overall survival and for non-complex/complex or GSA-/GSA+ patient comparisons.

Cox proportional hazard regression was used for univariate survival analysis. A  $p$ -value  $< 0.05$  was taken to represent a statistically significant difference between groups. In an exploratory analysis, we applied a Bayesian model to evaluate survival in subgroups with small sample sizes. For this, non-informative priors were assumed, and the Weibull distribution was used to model survival times with parameters estimated from the data. Markov Chain Monte Carlo sampling was used to generate posterior distributions for the survival probabilities. The posterior survival functions were plotted, and probabilities were compared between groups. Analyses were performed using IBM Statistical Package for the Social Sciences version 25 (SPSS Inc., Chicago, IL), with the stratification plot and Bayesian survival modelling performed using R version 4.3.2 (R Foundation, Vienna, Austria).

## Results

### Patient demographics, surgical anatomies, and non-anatomic substrates

During the study period, 86 patients were identified, with 3 patients who underwent redo-aortic arch repair excluded. The median follow-up time was 4.6 years (interquartile range: 3.3–10.3 years). Of the 83 included patients, 48.2% were male. The antenatal diagnosis had been made in 65.1% of patients. The median age at surgery was 8.0 days (interquartile range: 6–18 days); 68 patients were neonates (81.9%). The median weight at repair was 3.28 kg (interquartile range: 2.83–3.60 kg; Table 1). Five patients with complete atrioventricular canal all underwent primary arch repair+pulmonary artery banding with staged definitive intra-cardiac repair. A total of 13 patients (15.7%) had complex surgical lesions; these comprised 10 patients with double outlet right ventricle and/or transposition of great arteries and 3 additional patients requiring extensive bilateral PA reconstruction (1 with Williams syndrome; 1 with CHARGE syndrome; 1 with elastin gene mutation).

Concerning non-anatomical substrates, there was a high incidence of GSA+ patients ( $n = 27/83$ ; 32.5%). Thirteen patients (15.7%) were premature, 8 patients (9.6%) presented with preoperative shock, and 20 patients (24.1%) were mechanically ventilated pre-surgery. GSA+ patients had statistically more prematurity (29.6% vs. 8.9% in GSA- group;  $p = 0.02$ ); they also had significantly lower weight preoperatively with a median weight of 3.02 kg versus 3.38 kg in the GSA- patients ( $p = 0.01$ ; Table 1). There were no significant differences in preoperative characteristics in non-complex versus complex patients (Table 1). Notably, the incidence of preoperative shock or mechanical ventilation was similar in GSA- versus GSA+ or non-complex versus complex patients (Table 1) as were preoperative aortic arch segment dimensions (Supplementary Table 1).

### Intraoperative data, overall perioperative mortality, and morbidity

Median cardiopulmonary bypass and cross-clamp times for the entire cohort were 97.0 (IQR: 80.0–133.5) and 47.0 (interquartile range: 39.0–76.8), respectively (Table 2). Median cerebral perfusion time was 34.5 min (interquartile range: 29.0–40.0). Periods of deep hypothermic circulatory arrest were used in only 13 patients (interquartile range: 2–31 min;  $n = 5$  GSA+). Cardiopulmonary bypass and cross-clamp times were significantly longer for complex versus non-complex repairs (Table 2).

**Table 1.** Preoperative patient characteristics

		Non-complex	Complex	P-value	GSA-	GSA+	P-value
No. patients	83	70/83 (84.3)	13/83 (15.7)	N/A	56/83 (67.5)	27/83 (32.5)	N/A
Male gender	40/83 (48.2)	33/70 (47.1)	7/13 (53.9)	0.77	31/56 (55.4)	9/27 (33.3)	0.07
Premature	13/83 (15.7)	12/70 (17.1)	1/13 (7.7)	0.68	5/56 (8.9)	8/27 (29.6)	*0.02
Preoperative shock	8/83 (9.6)	6/70 (8.6)	2/13 (15.4)	0.60	5/56 (8.9)	3/27 (11.1)	0.71
Shones complex	10/83 (12.0)	9/70 (12.9)	1/13 (7.7)	1.00	6/56 (10.7)	4/27 (14.8)	0.72
Bicuspid AoV	15/83 (18.1)	15/70 (21.4)	0/13 (0.0)	0.11	11/56 (19.6)	4/27 (14.8)	0.76
DORV	8/83 (9.6)	0/70 (0.0)	8/13 (61.5)	N/A	8/56 (14.3)	0/27 (0.0)	0.05
Weight (kg)	3.28 (2.83–3.60)	3.25 (2.80–3.60)	3.40 (3.03–3.80)	0.45	3.38 (3.00–3.90)	3.02 (2.80–3.40)	*0.01
Age at surgery (days)	8.0 (6.0–18.0)	8.0 (6.0–16.0)	12.0 (8.5–32.0)	0.16	8.0 (6.0–16.5)	12.0 (7.0–24.0)	0.19
Antenatal diagnosis	54/82 (65.1)	45/70 (64.3)	9/13 (69.2)	0.08	35/56 (62.5)	21/27 (77.8)	0.21
Ventilated pre-surgery	20/83 (24.1)	17/70 (24.3)	3/13 (23.1)	1.00	10/56 (17.9)	10/27 (37.0)	0.10
GSA+	27/83 (32.5)	23/70 (32.9)	4/13 (30.8)	1.00	N/A	N/A	N/A
Complex lesion	13/83 (15.7)	N/A	N/A	N/A	9/56 (16.1)	4/27 (14.8)	1.00

Categorical variables: numbers (%); continuous variables: median (interquartile range).

AoV = aortic valve; VSD = ventricular septal defect; DORV = double outlet right ventricle; IAA = interrupted aortic arch; GSA = genetic/syndromic/extracardiac congenital anomaly; N/A = not applicable.

\* $p < 0.05$ .

Overall 30-day survival was 96.4%, with a hospital survival rate of 92.8% (Table 2). The 30-day and operative mortality was higher in complex versus non-complex patients, though this was not statistically significant (Table 2). In contrast, operative mortality was significantly greater in the GSA+ group (5/27: 18.5% vs. 1/56: 1.8%;  $p = 0.01$ ; Table 2). The stratification plot shown in Figure 1 helps to more clearly visualise the assignment of non-survivors with respect to surgical anatomic complexity and GSA status.

Concerning morbidity, 10 patients (12%) had postoperative pulmonary hypertension; 6 patients required mechanical circulatory support (7.2%). Occurrences of important neurological morbidity ( $n = 3$ ; 3.6%), sepsis ( $n = 2$ ; 2.4%), and renal failure ( $n = 1$ ; 1.2%) are shown in Table 2. Complex patients had a higher incidence of delayed sternal closure and requirement for mechanical circulatory support compared with non-complex patients (Table 2). GSA+ patients versus GSA- also had a higher mechanical circulatory support requirement and higher composite perioperative morbidity ( $p < 0.001$ ; Table 2).

#### Kaplan–Meier survival and Bayesian survival analysis

Overall Kaplan–Meier survival was 86.7% at 1, 5, and 10 years. Complex surgical patients had poorer Kaplan–Meier survival compared with those in the non-complex group ( $p = 0.01$ ; Figure 2a) as did those who were GSA+ versus GSA- ( $p < 0.001$ ; Figure 2b). Most of the attrition in these patients occurred within the first 60 days. The hazard ratios for death on univariate analysis (Table 3) were significant for both GSA+ status (HR 11.12, 95% CI 2.40–51.54;  $p = 0.002$ ) and complex anatomy (HR 7.95, 95% CI 2.42–26.13;  $p = 0.001$ ; Table 3). Bayesian modelling was used to further explore potential differences in survival attributable to complex anatomy and/or GSA+ status. This exploratory data analysis suggested similar detrimental effects on survival attributable to either complexity or being GSA+,

with the poorest outcomes in those with both risk factors (Figure 3a).

#### Modes of death in complex or GSA+ patients

At the completion of follow-up, 9 of 11 deaths were in GSA+ patients. There were no deaths in non-complex/GSA- patients. The 2 deaths in the GSA- group were both complex patients with double outlet right ventricle/transposition of great arteries who had undergone arterial switch operation, one of whom had a shock and was mechanically ventilated pre-repair; this patient also had interrupted aortic arch and concomitant repair of supracardiac total anomalous pulmonary venous connection. Both patients died within 3 months of surgery, and both had chylothorax (Supplementary Table 2). It is remarkable that the modes of death in the 9 GSA+ patients were mainly related to respiratory or neurological complications (Supplementary Table 2). This may partly have been related to the pre-repair need for mechanical ventilation in 7 of 9 of these patients, 5 of whom were premature, and 6 of 7 of whom had significant respiratory morbidity. Four GSA+ mortalities had important neurological complications, and this seemed directly related to the genetic syndrome in the 3 Dandy–Walker patients.

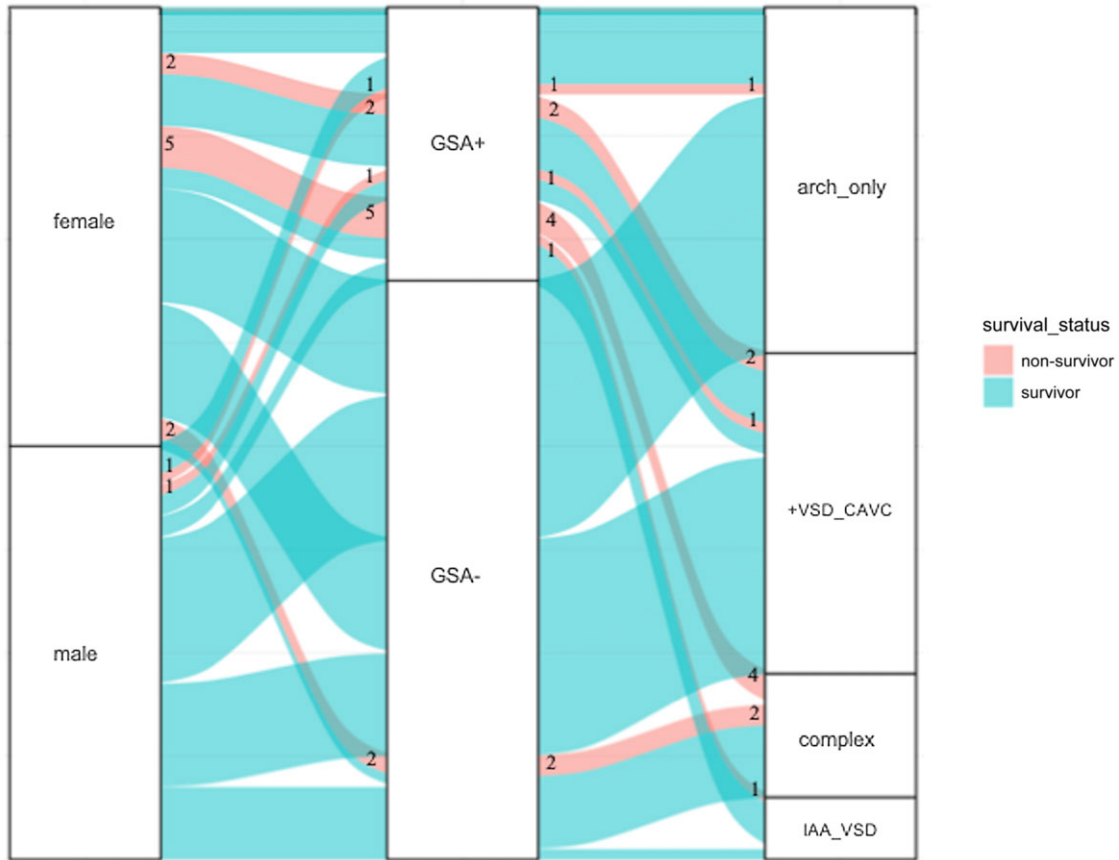
#### Arch and non-arch reinterventions

Postoperative arch dimensions and peak velocities were similar in complex versus non-complex and GSA- versus GSA+ patients (Supplementary Table 1). Kaplan–Meier freedom from arch reintervention was 90.3%, 87.7%, and 87.7% at 1, 5, and 10 years, respectively (Figure 3b). There was no significant difference in freedom from arch reintervention in complex versus non-complex ( $p = 0.27$ ; data not shown) or GSA+ versus GSA- (data not shown;  $p = 0.39$ ). There was also no significant difference in any of the post-repair arch dimensions in those with or without reinterventions (Figure 4a), and both groups had similar

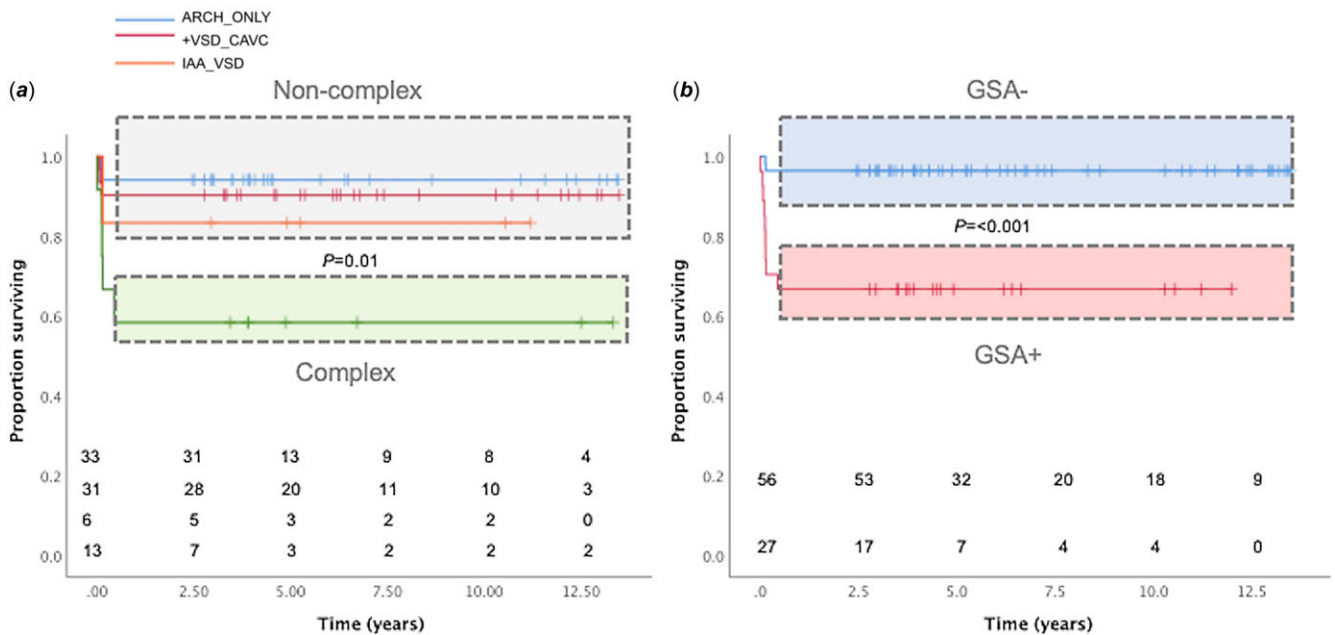
**Table 2.** Perioperative mortality and morbidity

		Non-complex	Complex	P-value	GSA-	GSA+	P-value
No. patients	83	70/83 (84.3)	13/83 (15.7)	N/A	56/83 (67.5)	27/83 (32.5)	N/A
30-day mortality	3/83 (3.6)	2/70 (2.9)	1/13 (7.7)	0.40	0/56 (0.0)	3/27 (11.1)	*0.03
Operative mortality	6/83 (7.2)	4/70 (5.7)	2/13 (15.4)	0.24	1/56 (1.8)	5/27 (18.5)	*0.01
Catheter_surgical arch reintervention	10/83 (12.0)	7/70 (10.0)	3/13 (23.1)	0.19	7/56 (12.5)	2/27 (7.4)	0.71
Delayed sternal closure	24/83 (28.9)	15/70 (21.4)	9/13 (69.2)	*0.001	14/56 (25.0)	10/27 (37.0)	0.31
Arrhythmia	18/83 (21.7)	14/70 (20.0)	4/13 (30.8)	0.46	13/56 (23.2)	5/27 (18.5)	0.78
Chylothorax	4/83 (4.8)	3/70 (4.3)	1/13 (7.7)	0.50	2/56 (3.6)	2/27 (7.4)	0.59
Mediastinal re-exploration	7/83 (8.4)	5/70 (7.1)	2/13 (15.4)	0.30	5/56 (8.9)	2/27 (7.4)	1.00
Re-intubation	6/83 (7.2)	5/70 (7.1)	1/13 (7.7)	1.00	2/56 (3.6)	4/27 (14.8)	0.08
>7 days mechanical ventilation	6/83 (7.2)	4/70 (5.7)	2/13 (15.4)	0.24	2/56 (3.6)	4/27 (14.8)	0.08
Drainage pleural effusion/pneumothorax	6/83 (7.2)	5/70 (7.1)	1/13 (7.7)	1.00	4/56 (7.1)	2/27 (7.4)	>0.99
Phrenic nerve paresis	3/83 (3.6)	3/70 (4.3)	0/13 (0.0)	1.00	3/56 (5.4)	0/27 (0.0)	0.55
Pulmonary hypertension	10/83 (12.0)	9/70 (12.9)	1/13 (7.7)	1.00	8/56 (14.3)	2/27 (7.4)	0.49
MCS	5/83 (6.0)	3/70 (4.3)	3/13 (23.1)	*0.046	0/56 (0.0)	5/27 (18.5)	*0.003
Neurological deficit	3/83 (3.6)	1/70 (1.4)	2/13 (15.4)	0.06	1/56 (1.8)	2/27 (7.4)	0.25
Sepsis	2/83 (2.4)	2/70 (2.9)	0/13 (0.0)	1.00	0/56 (0.0)	2/27 (7.4)	0.10
Renal failure	1/83 (1.2)	1/70 (1.4)	0/13 (0.0)	1.00	0/56 (0.0)	1/27 (3.7)	0.33
CPB time (min)	97.0 (80.5–133.5)	87.5 (79.0–113.0)	206.0 (146.8–270.3)	*<0.001	94.0 (79.5–131.5)	100.0 (82.3–134.3)	0.89
CCT (min)	47.0 (39.0–76.8)	44.5 (37.0–64.0)	132.0 (97.8–156.5)	*<0.001	49.0 (39.0–83.5)	45.0 (36.3–69.3)	0.48
Cerebral perfusion time (min)	34.5 (29.0–40.0)	34.0 (28.0–39.5)	36.5 (29.0–44.0)	0.46	34.0 (30.0–39.0)	35.5 (28.0–43.0)	0.97
Vocal cord paresis	22/82 (26.8)	19/70 (27.1)	3/13 (23.1)	1.00	13/56 (23.2)	9/27 (33.3)	0.43
PEG/G-Tube	10/83 (12.0)	10/70 (14.3)	1/13 (7.7)	1.00	5/56 (8.9)	5/27 (18.5)	0.28
Composite morbidity	16/83 (19.3)	10/70 (14.3)	4/13 (30.8)	0.22	4/56 (7.1)	12/27 (44.4)	*<0.001

MCS = mechanical circulatory support; CPB = cardiopulmonary bypass; CCT = cross-clamp time; PEG = percutaneous endoscopic gastrostomy/G (gastrostomy)-tube; composite morbidity = respiratory, neurological, sepsis, or renal failure combined end-point; GSA = genetic/syndromic/extracardiac congenital anomaly; N/A = not applicable. Categorical variables: numbers (percentage); continuous variables: median (interquartile range). \* $p < 0.05$ .



**Figure 1.** Stratification plot demonstrating assignment of survivors and non-survivors. The plot allows one to see at a glance the 11 mortalities in the cohort with respect to GSA, surgical complexity, and gender status. A pink line (non-survivors) may be followed from right to left in the plot (or vice versa), with the relative width of the line representing the number of patients (indicated for the respective lines). This plot may be viewed in conjunction with Supplementary Table 2. IAA = interrupted aortic arch; VSD = ventricular septal defect; CAVC = complete atrioventricular canal; GSA = genetic/syndromic/extracardiac congenital anomaly.



**Figure 2.** (a) Kaplan-Meier plot for survival according to surgical complexity. (b) Kaplan-Meier survival plot according to GSA status. Numbers at risk are shown on the respective plots. GSA = genetic/syndromic/extracardiac congenital anomaly; VSD = ventricular septal defect; CAVC = complete atrioventricular canal; IAA = interrupted aortic arch.

**Table 3.** Cox univariate analysis for mortality

	HR	95.0% CI		P-value
		Lower	Upper	
Gender	4.40	0.95	20.36	0.06
Prematurity	0.31	0.09	1.06	0.06
GSA+	11.12	2.4	51.54	*0.002
Ventilated pre-op	8.95	2.37	33.8	*0.001
Preoperative shock	4.2	1.11	15.85	*0.04
Complex lesion	7.95	2.42	26.13	*0.001

HR = hazard ratio; CI = confidence interval; GSA = genetic/syndromic/extracardiac congenital anomaly.

\* $p < 0.05$ .

postoperative median peak velocities across the arch with no clear clustering according to peak velocity or weight identifying those requiring arch reinterventions (Figure 4b).

Non-arch reinterventions included one patient with double outlet right ventricle requiring baffle revision for left ventricular outflow tract obstruction at 4 years; one patient with complex Yasui-arch repair (CHARGE syndrome) who had left ventricular outflow tract obstruction reoperation at 4 months; one right ventricular outflow tract revision (Taussig-Bing) at 6 weeks; and one left coronary artery/left pulmonary artery revision (Williams syndrome) at 2 days.

## Discussion

We have demonstrated favourable outcomes of neonatal and infant aortic arch repair in our recent cohort of patients with varied anatomic complexity. The salient finding of our study is that operative mortality was significantly adversely affected by GSA+ status, with continued post-discharge attrition significantly greater for both complex versus non-complex and GSA+ versus GSA- patients. Bayesian survival probability estimates were similar for complex/GSA- versus non-complex/GSA+ patients, with additive adverse effects on survival for these two risk factors. Non-complex/GSA- patients had 100% survival. Composite ICU morbidity was high in GSA+ patients, whilst reintervention rates were not influenced by either surgical complexity or GSA status.

The observed overall 30-day mortality of 3.6% and operative mortality of 7.2% compares favourably with the small number of contemporary studies that have reported outcomes of infant aortic arch repair.<sup>9</sup> Patukale *et al.* reported a recent single-centre series of aortic arch patch augmentation with 149 patients, although 48 patients were single ventricle repair, with an early mortality rate of 6%.<sup>10</sup> Others have reported perioperative mortality of 7–9.4%.<sup>11,12</sup>

In our series, anatomically complex patients exhibited continued attrition after hospital discharge as observed by others.<sup>13</sup> It is difficult, however, to disentangle the effects of surgical complexity from GSA status in other published data, although Mery *et al.* reported 4/30 deaths (13.3%; all GSA-) in complex biventricular arch repairs, all of whom had died by 3 months;<sup>14</sup> this compares with the death of 2 complex/GSA- out of 13 complex patients (15.4%) in our series. In a further report of 51 patients

undergoing arterial switch operation with aortic arch repair, early mortality was 9.8% with Kaplan–Meier 10-year freedom from death or transplant of 17.4%.<sup>15</sup> These authors did not report the prevalence of GSA+ patients, though they had a very low incidence of only 5.9% prematurity versus our cohort incidence of 15.7%.

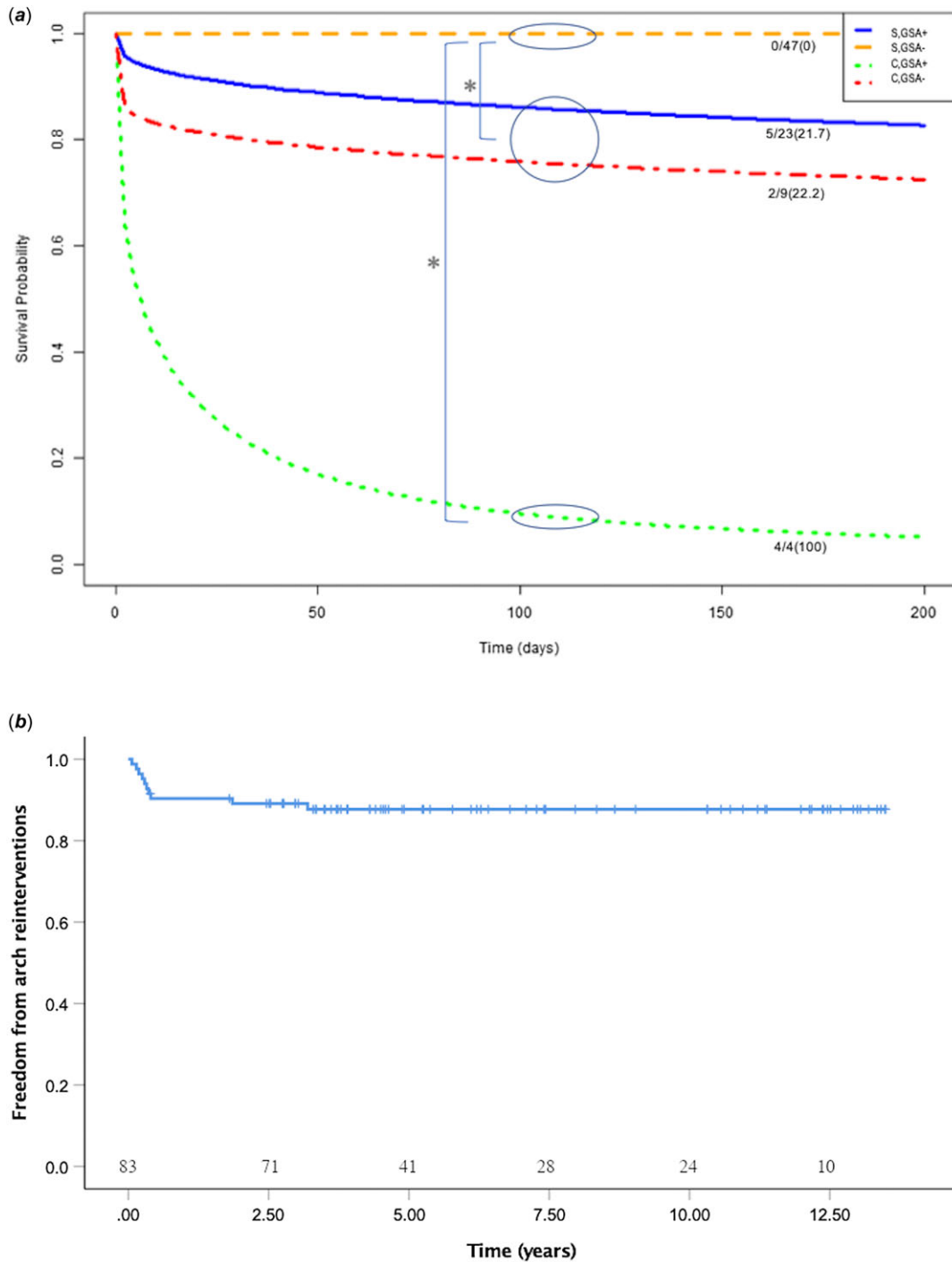
A wide variation in institutional incidence of GSAs has been reported, and the 32.5% incidence in our study cohort is in the upper range of the overall incidence reported for US institutions (90<sup>th</sup> percentile for GSA incidence 28–29%).<sup>16</sup> The few studies of infant arch repair that have documented GSA status in their patients have also demonstrated an increased risk of mortality and morbidity.<sup>14,17</sup> In a multicentre study of 1283 infants with interrupted aortic arch, patients with 22q11 deletion had a higher risk of morbidity, whereas those with complex cardiac anatomies or extracardiac or non-22q11 genetic syndromes exhibited higher mortality.<sup>2</sup> In our series, 23 of 27 GSA+ patients were non-22q11del, and this may partly explain the elevated mortality we observed in these patients.<sup>3</sup>

Of 11 patients who died in our overall cohort, 9 of 11 were GSA+. Hospital survival and post-discharge attrition were significantly worse in GSA+ versus GSA- patients, and these patients had higher morbidity (particularly respiratory and neurological) or need for mechanical circulatory support. In this regard, our findings are concordant with those of Mori and associates who also noted that neonates undergoing biventricular cardiac repairs who had prolonged ICU stays had a higher prevalence of GSAs with greater ICU morbidity and higher post-discharge mortality.<sup>13</sup> Immaturity of organ systems, immunologic incompetence, and lymphatic abnormalities are all potential mechanisms for higher morbidity and mortality in GSA+ patients.<sup>3</sup> The predisposition for poor neurological and neurodevelopmental outcomes is also of great concern for GSA+ patients, particularly those with Dandy–Walker syndrome,<sup>18</sup> all three of whom in our series died.

Our freedom from arch reintervention was 90.3% and 87.7% at 1 and 10 years; however, we did not observe any significant difference in reintervention rate for complex anatomic repairs or in GSA+ patients. Ghani *et al.* reported a freedom from reintervention of 89.4% at 1 year for 2-ventricle patients;<sup>11</sup> other series similarly report a 9–10% reintervention rate.<sup>9,19</sup> We believe that the consistent approach of aortic arch augmentation using pulmonary homograft patch even in complex anatomies such as transposition or double outlet right ventricle is reproducible. Notably, we did not have a single patient with bronchial compression. We were not able to predict which patients had reinterventions based on postoperative arch dimensions in contrast to a recent study.<sup>20</sup> Our rate of 2 of 83 (2.4%) left ventricular outflow tract obstruction reinterventions compares favourably with other reports.<sup>21</sup>

Our study has limitations of being a single-centre, retrospective study. Whilst focusing on biventricular repairs may have improved the homogeneity of our study cohort, the smaller resultant sample size may limit the strength of statistical inferences that have been made. The GSAs reported are varied in type for a relatively small number of patients, so differentiating effects of more common anomalies such as 22q11del or trisomy 21 from other genetic or extracardiac anomalies was not possible.

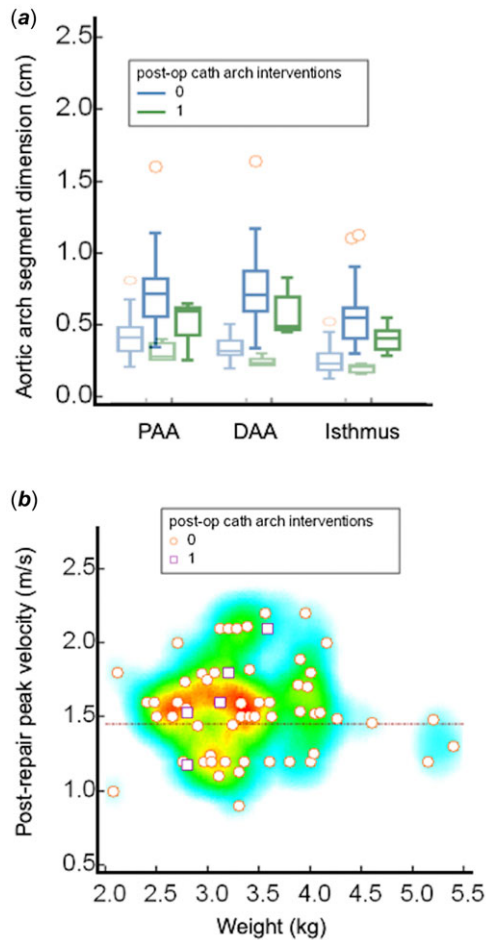
Although anatomic complexity, in contrast to GSA+ status, may have been somewhat neutralised as a risk factor for



**Figure 3.** (a) Bayesian survival model plot. The graph shows modelling according to 4 groups designated as S,GSA+; S,GSA-; C,GSA+; C,GSA-. Numbers (%) of patients who died in each subgroup are shown adjacent to the respective lines. \* indicates > 95% probability of a significant difference between the groups indicated. (b) Kaplan-Meier plot showing freedom from arch reinterventions according to the entire cohort. S = non-complex; C = complex; GSA = genetic/syndromic/extracardiac congenital anomaly.

operative mortality, there is further post-discharge attrition attributable to complexity and/or GSA+ status, with additive risk effects. Morbidity directly related to certain syndromes underlies some of this risk. Ultimately, advances in

understanding of the pathophysiologic mechanisms of ICU morbidity related to specific genetic aberrations may be required to identify targets to further optimise patient outcomes.



**Figure 4.** (a) Pre- and postoperative aortic arch segment dimensions and postoperative peak arch velocities at discharge. For arch dimensions, lighter bars represent the preoperative dimension with the paired adjacent darker bar showing the corresponding post-repair dimensions. Blue bars are for patients without arch reinterventions; green bars are for those who require arch reintervention. (b) Heatmap scatter plot demonstrating the relationship between post-repair peak arch velocity, weight, and arch reintervention status. PAA = proximal aortic arch; DAA = distal aortic arch. Medians with interquartile range are shown for (a).

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